



## HHS PUBLIC ACCESS

Author manuscript

*Gynecol Oncol.* Author manuscript; available in PMC 2016 December 01.

Published in final edited form as:

*Gynecol Oncol.* 2015 December ; 139(3): 401–406. doi:10.1016/j.ygyno.2015.09.080.

## A Preoperative Personalized Risk Assessment Calculator for Elderly Ovarian Cancer Patients undergoing Primary Cytoreductive Surgery

Emma L Barber, MD<sup>1</sup>, Sarah Rutstein, PhD<sup>2,3</sup>, William C Miller, MD, PhD<sup>3,4</sup>, and Paola A Gehrig, MD<sup>1,5</sup>

<sup>1</sup>University of North Carolina, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Chapel Hill, NC

<sup>2</sup>University of North Carolina, Department of Health Policy and Management, Gillings School of Public Health, Chapel Hill, NC

<sup>3</sup>University of North Carolina, Division of Infectious Diseases, Department of Internal Medicine, Chapel Hill, NC

<sup>4</sup>University of North Carolina, Department of Epidemiology, Gillings School of Public Health, Chapel Hill, NC

<sup>5</sup>Lineberger Clinical Cancer Center, University of North Carolina, Chapel Hill, NC

### Abstract

**Objective**—Cytoreductive surgery for ovarian cancer has higher rates of postoperative complication than neoadjuvant chemotherapy followed by surgery. If patients at high risk of postoperative complication were identified preoperatively, primary therapy could be tailored. Our objective was to develop a predictive model to estimate the risk of major postoperative complication after primary cytoreductive surgery among elderly ovarian cancer patients.

**Methods**—Patients who underwent primary surgery for ovarian cancer between 2005-2013 were identified from the National Surgical Quality Improvement Project. Patients were selected using primary procedure CPT codes. Major complications were defined as grade 3 or higher complications on the validated Claviden-Dindo scale. Using logistic regression, we identified demographic and clinical characteristics predictive of postoperative complication.

**Results**—We identified 2,101 ovarian cancer patients of whom 35.9% were older than 65. Among women older than 65, the rate of major postoperative complication was 16.4%. Complications were directly associated with preoperative laboratory values (serum creatinine,

Corresponding Author: Emma Barber, MD, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of North Carolina at Chapel Hill, 103B Physicians' Office Building, Campus Box #7572, Chapel Hill, NC 27599. Phone: 919-966-1194; Fax: 919-843-5387; [embarber@med.unc.edu](mailto:embarber@med.unc.edu).

Disclosure Statement: The authors report no conflict of interest.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

platelets, white blood cell count, hematocrit), ascites, white race, and smoking status, and indirectly associated with albumin. Our predictive model had an area under receiver operating characteristic curve of 0.725. In order to not deny patients necessary surgery, we chose a 50% population rate of postoperative complication which produced model sensitivity of 9.8% and specificity of 98%.

**Discussion**—Our predictive model uses easily and routinely obtained objective preoperative factors to estimate the risk of postoperative complication among elderly ovarian cancer patients. This information can be used to assess risk, manage postoperative expectations, and make decisions regarding initial treatment.

---

## Introduction

Primary cytoreductive surgery to no gross residual disease is associated with improved survival among patients with ovarian cancer.(1) The extensive cytoreductive effort that is required to debulk advanced ovarian cancer to no gross residual disease can be associated with major postoperative complication rates as high as 50%.(2) The elderly are known to be at a particularly high risk of postoperative complication after cytoreductive surgery and these complications impact morbidity and mortality.(3) In a study by Moore et al of octogenarians, death prior to hospital discharge and within 60 days of surgery occurred in 13% and 20% of cases, respectively and an additional 13% were unable to receive indicated postoperative therapy. The effects of postoperative complication can be farther-reaching than just morbidity and mortality related to surgery. Patients with postoperative complications experience delays in initiation of chemotherapy, may not be able to receive planned therapy, and experience subsequent decreased survival.(3, 4) Additionally, patients who receive neoadjuvant chemotherapy experience lower rates of postoperative complication compared to those who receive upfront cytoreductive surgery suggesting that neoadjuvant chemotherapy has the potential to decrease postoperative complications among patients at high risk.(2, 5)

Predictive models can provide a personalized assessment of the probability of a clinical event using patient specific characteristics and have increasingly been incorporated into the practice of oncology.(6, 7) Most oncologic predictive models require the input of demographic or disease specific variables and calculate the output of disease free or overall survival.(8, 9) In contrast, treatment-guiding predictive models can be helpful for clinical situations in which different options exist as treatment for a particular condition. In this scenario, outcomes from a predictive model give the user information that may influence their preference for a type of treatment. Ovarian cancer can be treated with either neoadjuvant chemotherapy or initial cytoreductive surgery making it particularly amenable to a predictive model.

Currently, neoadjuvant chemotherapy is the preferred therapy for ovarian cancer patients that have preoperatively identified unresectable disease, significant medical co-morbidities, or poor performance status. However, we do not currently have an accepted objective measure to determine which patients are least likely to benefit from an extensive cytoreductive effort. While many studies have focused on predicting the ability to resect

tumor to no gross residual disease, the patient's ability to tolerate surgery without significant morbidity is another important factor in triaging ovarian cancer patients for initial surgical management.(10, 11) If patients at high risk for postoperative complications could be identified preoperatively, patients and providers could use this information to personalize decisions regarding upfront surgical cytoreduction versus neoadjuvant chemotherapy.

Our objective was to create a novel predictive model to evaluate utility of readily available demographic and preoperative features to predict probability of postoperative complications among women greater than 65 years-old undergoing primary surgery for the treatment of ovarian cancer.

## Methods

### Study Population

Patients who underwent primary surgery for treatment of ovarian cancer from January 2005 through December 2013 and were recorded in the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) were included in this study. Patients were identified from the database for inclusion using the primary procedure Current Procedure Terminology (CPT) code. Only procedures with CPT codes that are specific to the initial treatment of ovarian cancer were included (58950, 58951, 58952, 58953, and 58954). The Institutional Review Board of the University of North Carolina at Chapel Hill reviewed this study and declared it exempt from formal review as it does not constitute human subjects research.

NSQIP is a national surgical quality program that provides risk-adjusted outcome measures for participating institutions to measure and improve the quality of care they deliver. Each entry in the database is an individual surgical procedure and includes variables associated with that surgical procedure. Specially trained nurses prospectively enter surgical case variables such as patient demographics, preoperative variables, intraoperative variables, and postoperative variables. Data is collected for the 30 days following surgery. The data is then de-identified of patient, hospital, and location-specific information and placed into the NSQIP database.(12)

### Measures

The outcome of interest, major postoperative complication, was a binary composite outcome and included all grade 3, 4 or 5 complications on the validated Clavien-Dindo scale(13) that are recorded in the NSQIP database. Major postoperative complications included myocardial infarction, pneumonia, venous thromboembolism, deep surgical site infection, stroke with neurologic deficit, unscheduled return to the operating room, renal failure, cardiopulmonary arrest, sepsis, intubation greater than 48 hours, or death. All outcomes were evaluated for 30 days postoperatively. More specific definitions of the criteria used to define each specific postoperative complication can found in the NSQIP data participant use file.(12) Only grade 3 complications and higher were included as these are complications that are sufficiently grave that patients and providers may alter plans for type of initial treatment if they had preoperative knowledge that these outcomes were likely.

Potential predictors of major complications were identified based on the current literature that suggests that certain preoperative characteristics are associated with postoperative complication. In addition, predictors had to be easy to assess preoperatively and objective in order to decrease intra-observer variability, subjectivity, and increase ease of use in the clinical setting. Objective numerical variables such as laboratory values or categorical variables with little intra-observer variability were preferentially included. Variables such as American Society of Anesthesiologist (ASA) scores, which are likely associated with complications, were not included as they require the user to determine the ASA score preoperatively which hinders the ease of use of the score. Both age and BMI have been associated with complications among gynecologic oncology patients(11, 14). Low albumin, low hematocrit, elevated creatinine, and thrombocytopenia are associated with poor performance status and have been associated with complications among a diversity of surgical patients(15-21). In regard to cancer biology, both white blood cells and platelets have been linked to aggressive cancer biology, poor prognosis, and postoperative complications among ovarian cancer patients(22-25). The predictors of major complication that we investigated included patient demographics, including age and race; preoperative laboratory values, including platelet count, white blood cell count, creatinine, albumin, and hematocrit; and patient comorbidities, including diabetes, hypertension, chronic obstructive pulmonary disease (COPD), myocardial infarction (MI) within 6 months, history of cerebrovascular accident (CVA) and history of transient ischemic attack (TIA). These comorbidities were defined as per the NSQIP user guide.(26)

### Statistical Analyses

We developed a predictive model using multiple logistic regression restricted to persons in the dataset greater than 65 years of age. This elderly-focused analysis was driven by previous studies that have found a direct relationship between age and postoperative complications and mortality in ovarian cancer patients undergoing cytoreductive surgery and that patients receiving neoadjuvant chemotherapy are older than those receiving primary debulking surgery (11, 27-30). Additionally, the predictors of major complication may be different between young and old patients and the median age at ovarian cancer diagnosis is 63 years of age. Thus, we decided to examine the subset of our population that would be more likely to receive neoadjuvant chemotherapy and more likely to have a postoperative complication. We first conducted bivariate analyses with predictor variables hypothesized to be associated with major postoperative complication. We used Akaike's information criteria (AIC) to identify appropriate functional form for each variable(31), testing linear, quadratic, categorical, binary, and in some cases restricted quadratic splines according to the observed distribution of the predictor variable.

The model was composed of a priori identified demographics and preoperative clinical variables with bivariate p-values <0.5. This high threshold was chosen to ensure that available important predictors were not excluded.(32) Investigated variables that did not meet this bivariate p-value threshold of  $p < 0.5$  were not included in the predictive model.

All variables were included based on hypothesized associations that were confirmed in bivariable analyses. The anticipated implementation of this risk score is the creation of a tool

by which clinicians could input the predictors into a computer program that would calculate the predicted probability of a major postoperative complication. Therefore, there is no cost to the inclusion of all of the predictor variables and we did not reduce the model with backwards elimination after variables were identified as appropriate for inclusion based on bivariable analyses.

We assessed the area under the receiver operating characteristic curves (AUROC) for each model (chi-squared test).(33) AUROC is a measure of an algorithm's discriminatory power – where 1.0 indicates a perfect test (i.e., 100% sensitivity and 100% specificity).(34) Model calibration was assessed using Hosmer-Lemeshow (HL) goodness-of-fit tests.(35) All analyses were conducted using Stata statistical software (Version 13.0; Stata Corporation, College Station, TX).

## Results

### Study population

We identified 2,101 patients who underwent primary surgery for the treatment of ovarian cancer and 35.9% (n=751) were older than 65 years old. These 751 women comprised our study population. Demographic and preoperative characteristics for all patients as well as only those greater than 65 years old are listed in Table 1 for comparison purposes. The rate of major complication was 12.3% for the full population and 16.4% among women older than 65 years old.

### Bivariable analyses

We compared elderly patients with major complication to those without to determine associations with demographic or preoperative variables. Patients older than 65 years old who experienced a major complication were more likely to have ascites ( $p<0.0001$ ) compared to those without a major complication. They also had lower preoperative albumin ( $p<0.0001$ ) as well as higher preoperative white blood cell counts ( $p=0.009$ ) and serum creatinine levels ( $p=0.003$ ) (Table 2).

### Multivariable analyses

Investigated variables associated with major postoperative complication in bivariable analysis with a  $p$ -value $<0.5$  were included in the predictive model and included preoperative creatinine, preoperative platelet count, preoperative hematocrit, preoperative white blood cell count, preoperative albumin, ascites, smoking status, and a binary indicator of race (white vs non-white) (Table 3). Investigated variables that did not meet the criteria of  $p<0.5$  and thus were not included in the predictive model included age, BMI, hypertension, diabetes, COPD, MI, CVA, and TIA. Predictors associated with major complication on bivariable analysis were then placed in a multivariable logistic regression model to evaluate predictors associated with the outcome of major complication (Supplementary Table 1). The full model included 8 predictor variables (AUROC=0.725) (Figure 1). The HL calibration test failed to reject the null hypothesis that there was a statistically significant difference between observed and predicted estimates ( $p=0.53$ ) meaning that the predicted and observed estimate are similar and the model is predictive.

Another way to evaluate the performance of this algorithm is examination of the algorithm's sensitivity and specificity at various clinically-relevant thresholds. In this scenario, the outcome (predicted probability of major complication) is treated as a binary event rather than a probability or percentage. For example, for patients with a 35% predicted probability of experiencing a complication, our algorithm is 21.8% sensitive and 92.6% specific. Put another way, using a threshold of 35% probability of complication, we would capture approximately 20% of the total population of women who will experience a complication. At a threshold of 50% probability of experiencing a major complication, the sensitivity drops to 9.8%, so only capturing approximately 10% of women who will experience this outcome, but specificity is 98.0%. Thus, we accurately classify the vast majority of women who will *not* experience a complication.

We set the rate of major postoperative complication at a rate that is reflected in the current literature, which varies between 9% and 52.6%.<sup>(2, 5, 36, 37)</sup> Given this large range, we elected to use a higher rate of postoperative complication as we did not want the model output to prevent patients from obtaining surgery who would otherwise benefit from it. Put another way, we desired a high specificity for our model and only wanted to predict postoperative complication for patients who were highly likely to experience one. This is because when the model is used in clinical practice, we want the plan for upfront cytoreductive surgery to only be altered if the probability of a major postoperative complication and resulting morbidity and mortality is high.

## Discussion

We have developed a predictive model using standard and readily available objective preoperative factors to predict major postoperative complication among elderly ovarian cancer patients. This model can be used as a risk assessment tool, similar to the Gail model for breast cancer, in which the clinician and/or patient input the preoperative factors and the model output is displayed as a probability that the specific patient experiences a postoperative complication. All model inputs are empirical and straightforward to assess preoperatively, in fact, most are objective numbers such as laboratory values.

Prior studies have identified factors that are associated with postoperative complication among ovarian cancer patients. Studies have found that older age, poor nutrition status, and stage IV disease are associated with postoperative complication.<sup>(3, 11, 38)</sup> A recent study using NSQIP data to examine ovarian cancer patients found that greater than three extended procedures is a stronger risk factor for postoperative complication than demographic or clinical factors.<sup>(39)</sup> Our study differs from this study in a number of ways. Our goal was to develop a predictive model that can be used as a pre-operative tool by clinicians and patients and that drove our methodology. This led us to select a higher risk population by including only patients greater than 65 years of age as this is the population that gynecologic oncologists most often consider neoadjuvant chemotherapy in. We also only included variables that are known preoperatively in our model, as although the number of surgical procedures performed at the time of cytoreductive effort maybe an important risk factor, the true number of procedures required will not be known until the time of surgery at which point the information can no longer be used to make decisions regarding initial treatment.



In order to best select the subgroup of patients that will benefit from upfront cytoreductive surgery versus neoadjuvant chemotherapy, much attention has been focused on developing predictive models to assess which patients will be able to be cytoreduced to no gross residual disease. Models using CA125, CT scans, and laparoscopy have all been employed. (10, 40-42) All of these models have one thing in common: the desire to transform something potentially subjective to an objective measurable score. While the ability to achieve resection to no gross residual disease is an important factor in selecting primary treatment for ovarian cancer, the patient's likelihood of experiencing a major postoperative complication is another important factor. Patients who experience major complications experience morbidity and mortality related to their complications, reductions in quality of life, and chemotherapy delays, which can result in compromised survival.(3, 4) Aletti et al performed a multicenter study, which found a subgroup of patients with older age, poor performance or nutritional status, and disseminated disease among whom the benefits of extensive surgical efforts do not outweigh the risks.(11) These patients had a 63.6% risk of postoperative morbidity and a decreased survival (17 months versus 27 months) associated with extensive cytoreductive efforts. Currently, in clinical practice, a combination of patient comorbidities, age, and functional status are used to decide between neoadjuvant chemotherapy and upfront cytoreductive surgery, however, much of this is subjective. Just as the aforementioned cytoreductive scores inject objectivity into the question of whether optimal cytoreductive surgery can be performed, our predictive model allows surgeons to use easily obtained preoperative data to objectively assess the possibility of a postoperative complication and resulting morbidity.

Our predictive model can be used in two ways – either as a quantitative model which displays the output of major complication as a probability for the individual patient or as a predictor of a binary event, that the patient experiences or does not experience a major complication. In the quantitative model, the model output is the risk or continuous probability that the patient experiences a major complication. Our quantitative model has reasonable discriminatory power with an AUROC of 0.725.

When the model is used to predict a binary outcome, we classify the postoperative complication outcome as a binary event, rather than a continuous probability. In this version, the specificity is high at 98%, meaning that we will accurately identify 98% of patients who will not experience a postoperative complication. The high specificity of the model is particularly useful clinically. It means that upfront cytoreductive surgery is the standard for all patients whom a physician would normally operate on and that the predictive model only indicates that a patient will experience a postoperative complication if that outcome is highly likely. For example, when used in clinical practice, the user would input the model predictors and a postoperative major complication would be either predicted or not predicted. If a major complication is not predicted, surgery can proceed, as the probability of a major complication is very low (specificity of 98%). If a major complication is predicted, the patient and provider should assess comorbidities, the likelihood of achieving optimal cytoreduction and determine if the risk of oncologic benefit outweighs the risk of postoperative morbidity. In this scenario, the quantitative model may be helpful to quantitate the risk of postoperative morbidity and guide decision-making.

Our predictive model uses the inputs of preoperative serum creatinine, platelet count, preoperative hematocrit, white blood cell count, albumin, as well as ascites, current smoking, and race to estimate the probability that a specific patient experiences a postoperative complication. Increasingly in medicine we are moving towards individualized medicine where care is tailored to fit the patient. Quality and reproducibility in medical care have also gained increasing prominence. Currently, we have no accepted method for quantifying surgical risk in patients undergoing surgery for ovarian cancer and so there is great variation in physician practice patterns. By providing patients and their surgeons with a patient-specific quantitative risk probability, this calculator could help to both individualize and standardize the initial treatment of ovarian cancer.

Patient autonomy and quality of life are important for patients. Increasing attention has been paid to patient preferences with the accepted concept that it is not just quantity of life but the quality of life that is important to patients. This concept is especially important in the geriatric oncology population as these patients often present with “multimorbidity”. Multimorbidity is the concept that older patients often present with multiple overlapping chronic conditions and that a practical and rationale approach must be taken to treating these patients as clinical practice guidelines are often not tailored to these complicated patients.(43) If elderly patients were provided with the output of our model and therefore an individualized assessment of the likelihood that they would experience a major complication after surgery for ovarian cancer it would enhance their ability to participate in shared decision-making regarding their initial treatment. We know that postoperative complications are associated with longer hospitalizations and decreased quality of life. Patients armed with the information that they are at high risk of a major complication might decide to defer initial surgical management in favor of neoadjuvant chemotherapy.

Limitations of our study include those that pertain to the use of a large national quality database. Data on cancer specific variables are missing from the NSQIP database and so we cannot use stage or CA125 levels in our models for postoperative complication. Additionally, selection of patients was based on CPT codes and we cannot exclude the possibility of miscoding or misclassification. However, in contrast to large databases, which utilize billing and coding data only, the NSQIP database is prospectively collected by trained personnel for the purpose of surgical quality and perioperative complication measurement.(12) NSQIP only records post-operative data for 30 days after surgery and thus our complication rates do not include events, which occurred after that time point and therefore we may have underestimated the true risk of postoperative complication. Additionally, by definition, the NSQIP database only included patients who underwent surgery for the treatment of ovarian cancer and have therefore been deemed fit enough by a surgeon to enter the operating room. Some of the same factors that we use in our risk calculator such as age and other markers of medical comorbidity may have been used by the surgeons in this study preoperatively to make a decision not to operate and thus the true rate of postoperative complication in an unselected population may actually be higher. The high rate of postoperative complication that we selected in our binary output model minimizes these limitations. Lastly, this predictive model was specifically developed in a cohort of elderly ovarian cancer patients and cannot be extrapolated to predict complications among patients less than 65 years old.



We have developed a predictive model to estimate the risk of postoperative complication among elderly patients undergoing primary surgery for the treatment of ovarian cancer based on easily obtained objective preoperatively-known factors. Postoperative complication is associated with morbidity, decreased quality of life, delay in receipt of chemotherapy, and mortality. The information from this model can be used by patients and providers to help them assess risk, manage postoperative expectations, and make decisions regarding initial treatment.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

Financial Support: Dr Barber is supported by NIH 5T32 HD040672-15.

## References

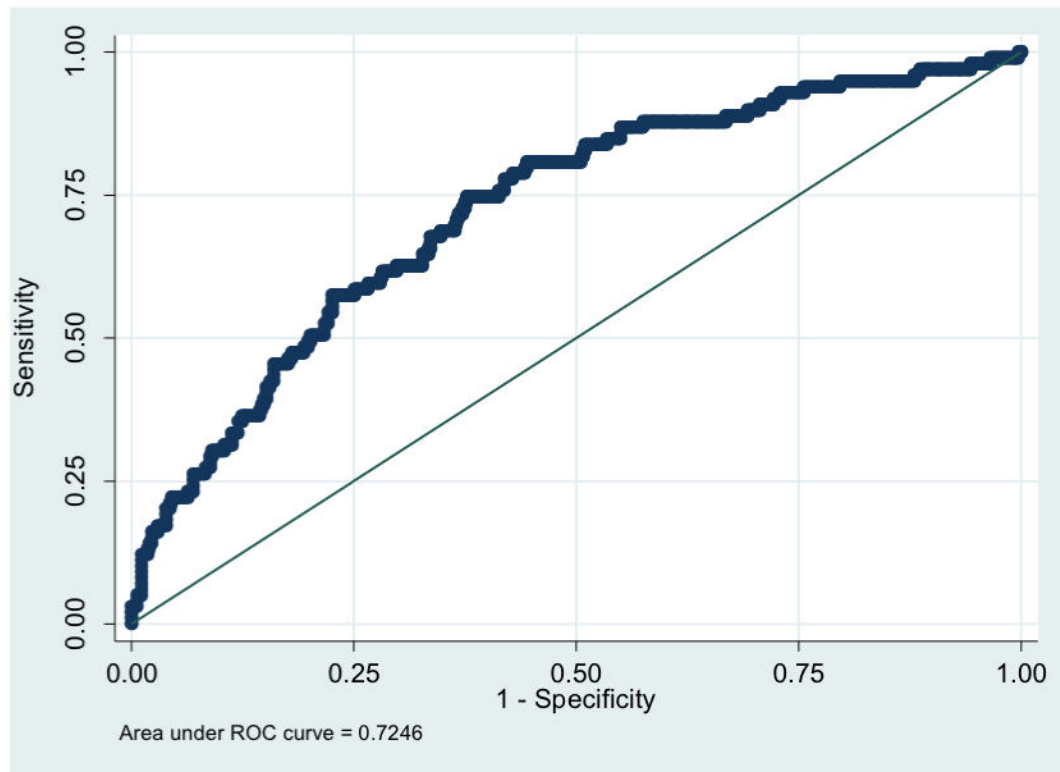
1. Chang SJ, Hodeib M, Chang J, Bristow RE. Survival impact of complete cytoreduction to no gross residual disease for advanced-stage ovarian cancer: a meta-analysis. *Gynecologic oncology*. 2013; 130(3):493–8. [PubMed: 23747291]
2. Fagotti, A.; Vizzielli, G.; Fanfani, F.; Chiantera, V.; Margariti, PA.; Gallota, V.; Costantini, B.; Ferrandina, G.; Tortorella, L.; Scambia, G. Society of Gynecologic Oncology. Chicago, IL: 2015. Phase III SCORPION trial (ID number: NCT01461850) in epithelial ovarian cancer patients with high tumor load receiving PDS versus NACT: An interim analysis on peri-operative outcome.
3. Moore KN, Reid MS, Fong DN, Myers TK, Landrum LM, Moxley KM, et al. Ovarian cancer in the octogenarian: does the paradigm of aggressive cytoreductive surgery and chemotherapy still apply? *Gynecologic oncology*. 2008; 110(2):133–9. [PubMed: 18495221]
4. Wright JD, Herzog TJ, Neugut AI, Burke WM, Lu YS, Lewin SN, et al. Effect of radical cytoreductive surgery on omission and delay of chemotherapy for advanced-stage ovarian cancer. *Obstetrics and gynecology*. 2012; 120(4):871–81. [PubMed: 22996105]
5. Vergote I, Trope CG, Amant F, Kristensen GB, Ehlen T, Johnson N, et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *The New England journal of medicine*. 2010; 363(10):943–53. [PubMed: 20818904]
6. Graefen M, Karakiewicz PI, Cagiannos I, Quinn DI, Henshall SM, Grygiel JJ, et al. International validation of a preoperative nomogram for prostate cancer recurrence after radical prostatectomy. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*. 2002; 20(15):3206–12. [PubMed: 12149292]
7. Hyman DM, Eaton AA, Gounder MM, Smith GL, Pamer EG, Hensley ML, et al. Nomogram to predict cycle-one serious drug-related toxicity in phase I oncology trials. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*. 2014; 32(6):519–26. [PubMed: 24419130]
8. Karakiewicz PI, Briganti A, Chun FK, Trinh QD, Perrotte P, Ficarra V, et al. Multi-institutional validation of a new renal cancer-specific survival nomogram. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*. 2007; 25(11):1316–22. [PubMed: 17416852]
9. Stephenson AJ, Scardino PT, Eastham JA, Bianco FJ Jr, Dotan ZA, DiBlasio CJ, et al. Postoperative nomogram predicting the 10-year probability of prostate cancer recurrence after radical prostatectomy. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*. 2005; 23(28):7005–12. [PubMed: 16192588]
10. Suidan RS, Ramirez PT, Sarasohn DM, Teitcher JB, Mironov S, Iyer RB, et al. A multicenter prospective trial evaluating the ability of preoperative computed tomography scan and serum CA-125 to predict suboptimal cytoreduction at primary debulking surgery for advanced ovarian,

- fallopian tube, and peritoneal cancer. *Gynecologic oncology*. 2014; 134(3):455–61. [PubMed: 25019568]
11. Aletti GD, Eisenhauer EL, Santillan A, Axtell A, Aletti G, Holschneider C, et al. Identification of patient groups at highest risk from traditional approach to ovarian cancer treatment. *Gynecologic oncology*. 2011; 120(1):23–8. [PubMed: 20933255]
  12. American College of Surgeons National Surgical Quality Improvement Program User Guide. Chicago, IL: American College of Surgeons; 2008.
  13. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Annals of surgery*. 2004; 240(2): 205–13. [PubMed: 15273542]
  14. Kumar A, Bakkum-Gamez JN, Weaver AL, McGree ME, Cliby WA. Impact of obesity on surgical and oncologic outcomes in ovarian cancer. *Gynecologic oncology*. 2014; 135(1):19–24. [PubMed: 25110330]
  15. Glance LG, Blumberg N, Eaton MP, Lustik SJ, Osler TM, Wissler R, et al. Preoperative thrombocytopenia and postoperative outcomes after noncardiac surgery. *Anesthesiology*. 2014; 120(1):62–75. [PubMed: 23903021]
  16. Squires MH 3rd, Lad NL, Fisher SB, Kooby DA, Weber SM, Brinkman A, et al. The Effect of Preoperative Renal Insufficiency on Postoperative Outcomes after Major Hepatectomy: A Multi-Institutional Analysis of 1,170 Patients. *Journal of the American College of Surgeons*. 2014
  17. Roses RE, Tzeng CW, Ross MI, Fournier KF, Abbott DE, You YN. The palliative index: predicting outcomes of emergent surgery in patients with cancer. *Journal of palliative medicine*. 2014; 17(1):37–42. [PubMed: 24410420]
  18. Kathiresan AS, Brookfield KF, Schuman SI, Lucci JA 3rd. Malnutrition as a predictor of poor postoperative outcomes in gynecologic cancer patients. *Archives of gynecology and obstetrics*. 2011; 284(2):445–51. [PubMed: 20803205]
  19. Maxwell MJ, Moran CG, Moppett IK. Development and validation of a preoperative scoring system to predict 30 day mortality in patients undergoing hip fracture surgery. *British journal of anaesthesia*. 2008; 101(4):511–7. [PubMed: 18723517]
  20. Dunne JR, Malone D, Tracy JK, Gannon C, Napolitano LM. Perioperative anemia: an independent risk factor for infection, mortality, and resource utilization in surgery. *The Journal of surgical research*. 2002; 102(2):237–44. [PubMed: 11796024]
  21. Amrock LG, Neuman MD, Lin HM, Deiner S. Can routine preoperative data predict adverse outcomes in the elderly? Development and validation of a simple risk model incorporating a chart-derived frailty score. *Journal of the American College of Surgeons*. 2014; 219(4):684–94. [PubMed: 25154667]
  22. Stone RL, Nick AM, McNeish IA, Balkwill F, Han HD, Bottsford-Miller J, et al. Paraneoplastic thrombocytosis in ovarian cancer. *The New England journal of medicine*. 2012; 366(7):610–8. [PubMed: 22335738]
  23. Allensworth SK, Langstraat CL, Martin JR, Lemens MA, McGree ME, Weaver AL, et al. Evaluating the prognostic significance of preoperative thrombocytosis in epithelial ovarian cancer. *Gynecologic oncology*. 2013; 130(3):499–504. [PubMed: 23747328]
  24. So KA, Hong JH, Jin HM, Kim JW, Song JY, Lee JK, et al. The prognostic significance of preoperative leukocytosis in epithelial ovarian carcinoma: a retrospective cohort study. *Gynecologic oncology*. 2014; 132(3):551–5. [PubMed: 24440470]
  25. Barber, EL.; Boggess, JB.; Van Le, L.; Kenneth, KH.; Bae-Jump, VL.; Brewster, WR.; Soper, JT.; Gehrig, PA. Society of Gynecologic Oncology. Chicago, IL: Mar. 2015 Preoperative Thrombocytosis and Leukocytosis in Ovarian Cancer Patients is Associated with 30-day Postoperative Death. Featured Poster Presentation.
  26. Program ACoSNSQI. American College of Surgeons National Surgical Quality Improvement Program. Chicago, IL: American College of Surgeons; ACS-NSQIP user guide for the 2011 participant use data file.
  27. Alphs HH, Zahurak ML, Bristow RE, Diaz-Montes TP. Predictors of surgical outcome and survival among elderly women diagnosed with ovarian and primary peritoneal cancer. *Gynecologic oncology*. 2006; 103(3):1048–53. [PubMed: 16876237]

28. Janda M, Youlden DR, Baade PD, Jackson D, Obermair A. Elderly patients with stage III or IV ovarian cancer: should they receive standard care? *International journal of gynecological cancer: official journal of the International Gynecological Cancer Society*. 2008; 18(5):896–907. [PubMed: 17986243]
29. Aletti GD, Dowdy SC, Podratz KC, Cliby WA. Relationship among surgical complexity, short-term morbidity, and overall survival in primary surgery for advanced ovarian cancer. *American journal of obstetrics and gynecology*. 2007; 197(6):676 e1–7. [PubMed: 18060979]
30. Rosen B, Laframboise S, Ferguson S, Dodge J, Bernardini M, Murphy J, et al. The impacts of neoadjuvant chemotherapy and of debulking surgery on survival from advanced ovarian cancer. *Gynecologic oncology*. 2014; 134(3):462–7. [PubMed: 25026637]
31. Pan W. Akaike's information criterion in generalized estimating equations. *Biometrics*. 2001; 57(1):120–5. [PubMed: 11252586]
32. Sun GW, Shook TL, Kay GL. Inappropriate use of bivariable analysis to screen risk factors for use in multivariable analysis. *Journal of clinical epidemiology*. 1996; 49(8):907–16. [PubMed: 8699212]
33. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics*. 1988; 44(3):837–45. [PubMed: 3203132]
34. Deeks JJ. Systematic reviews in health care: Systematic reviews of evaluations of diagnostic and screening tests. *Bmj*. 2001; 323(7305):157–62. [PubMed: 11463691]
35. Hosmer, D.; Lemeshow, S. *Applied Logistic Regression*. 2nd. John Wiley & Sons, Inc; 2000.
36. Chi DS, Franklin CC, Levine DA, Akselrod F, Sabbatini P, Jarnagin WR, et al. Improved optimal cytoreduction rates for stages IIIC and IV epithelial ovarian, fallopian tube, and primary peritoneal cancer: a change in surgical approach. *Gynecologic oncology*. 2004; 94(3):650–4. [PubMed: 15350354]
37. Aletti GD, Dowdy SC, Gostout BS, Jones MB, Stanhope CR, Wilson TO, et al. Aggressive surgical effort and improved survival in advanced-stage ovarian cancer. *Obstetrics and gynecology*. 2006; 107(1):77–85. [PubMed: 16394043]
38. Stashwick C, Post MD, Arruda JS, Spillman MA, Behbakht K, Davidson SA, et al. Surgical risk score predicts suboptimal debulking or a major perioperative complication in patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer. *International journal of gynecological cancer: official journal of the International Gynecological Cancer Society*. 2011; 21(8):1422–7. [PubMed: 21997170]
39. Patankar S, Burke WM, Hou JY, Tergas AI, Huang Y, Ananth CV, et al. Risk stratification and outcomes of women undergoing surgery for ovarian cancer. *Gynecologic oncology*. 2015; 138(1): 62–9. [PubMed: 25976399]
40. Kang S, Park SY. To predict or not to predict? The dilemma of predicting the risk of suboptimal cytoreduction in ovarian cancer. *Annals of oncology: official journal of the European Society for Medical Oncology / ESMO*. 2011; 22(Suppl 8):viii23–viii8. [PubMed: 22180395]
41. Fagotti A, Vizzielli G, De Iaco P, Surico D, Buda A, Mandato VD, et al. A multicentric trial (Olympia-MITO 13) on the accuracy of laparoscopy to assess peritoneal spread in ovarian cancer. *American journal of obstetrics and gynecology*. 2013; 209(5):462 e1–e11. [PubMed: 23891632]
42. Fanfani F, Monterossi G, Fagotti A, Gallotta V, Costantini B, Vizzielli G, et al. Positron emission tomography-laparoscopy based method in the prediction of complete cytoreduction in platinum-sensitive recurrent ovarian cancer. *Annals of surgical oncology*. 2015; 22(2):649–54. [PubMed: 25155399]
43. Thompson K, Dale W. How do I best manage the care of older patients with cancer with multimorbidity? *Journal of geriatric oncology*. 2015; 6(4):249–53. [PubMed: 26149516]

### Highlights

- A preoperative risk assessment tool predicts major postoperative complication among elderly ovarian cancer patients undergoing cytoreductive surgery.
- This risk assessment tool can be used by clinicians and patients to help make decisions regarding initial ovarian cancer treatment.



**Figure 1. Area Under the Receiver Operator Curve (AUROC) for Regression Model**

The area under an ROC curve is a measure of model performance. Specifically, the area measures discrimination – in this case the ability of the predictive model to correctly classify persons with and without postoperative complication. The observed AUROC for this model was 0.725.

**Table 1**  
**Population Characteristics**

	Overall (n=2,101)	Women >65yo (n=751, 35.7%)
Age (years)		
65	1343 (63.9)	0 (0.0)
66 – 70	292 (13.9)	292 (38.9)
71 – 80	352 (16.8)	352 (46.9)
81 - 90	107 (5.1)	107 (14.2)
BMI (kg/m <sup>2</sup> )		
< 18.5	48 (2.3)	17 (2.3)
18.5 – 24.9	645 (30.7)	262 (34.9)
25 – 29.9	581 (27.7)	242 (32.2)
30 – 34.9	392 (18.7)	133 (17.7)
35 – 39.9	218 (10.4)	55 (7.3)
40	190 (9.0)	36 (4.8)
Unknown	21 (1.6%)	6 (0.8%)
Race		
White	1563 (74.4)	590 (78.6)
Black	194 (9.2)	52 (6.9)
Asian	91 (4.3)	25 (3.3)
Unknown	253 (12.1)	84 (11.2)
Hypertension requiring medication		
Yes	901 (42.9)	454 (60.5)
No	1200 (57.1%)	297 (39.5)
Smoker		
Yes	319 (15.2)	61 (8.1)
No	1782 (84.8)	690 (91.9)
Insulin-Dependent Diabetes		
Yes	247 (11.8)	99 (13.2)
No	1854 (88.2)	652 (86.8)
History of severe COPD		
Yes	58 (2.8)	36 (4.8)
No	2043 (97.2)	258 (95.2)
History of CVA		
Yes	6 (0.3)	3 (0.4)
No	2095 (99.7)	748 (99.6)
MI within 6 months		
Yes	2 (0.1)	1 (0.1)



	<b>Overall (n=2,101)</b>	<b>Women &gt;65yo (n=751, 35.7%)</b>
No	2099 (99.9)	750 (99.9)
History of TIA		
Yes	12 (0.6)	11 (1.5)
No	2089 (99.4)	740 (98.5)
Preoperative creatinine (mg/dL)		
< 1.5	1869 (89.0)	681 (90.7)
1.5	61 (2.9)	34 (4.5)
Unknown	171 (8.1)	36 (4.8)
Preoperative hematocrit (%)		
< 30	163 (7.8)	67 (8.9)
30	1853 (88.2)	664 (88.4)
Unknown	85 (4.0)	20 (2.7)
Preoperative platelet count (10 <sup>9</sup> /L)		
< 450		
450	1823 (86.8)	666 (88.7)
Unknown	199 (9.5)	66 (8.8)
	79 (3.8)	19 (2.5)
Preoperative white blood cell count (10 <sup>9</sup> /L)		
< 10	1628 (77.5)	606 (80.7)
10	393 (18.7)	123 (16.4)
Unknown	80 (3.8)	22 (2.9)
Preoperative albumin (g/dL)		
< 3.5	345 (16.4)	153 (20.4)
3.5	1079 (51.4)	391 (52.1)
Unknown	677 (32.3)	207 (27.6)
Ascites		
Yes	407 (19.4)	164 (21.8)
No	1694 (80.6)	587 (78.2)

Data is reported as n(%). BMI (body mass index), chronic obstructive pulmonary disease (COPD), myocardial infarction (MI), cerebrovascular accident (CVA), and transient ischemic attack (TIA). Bolded text indicates statistical significance with  $p < 0.05$ .

**Table 2**  
**Bivariable Associations for Elderly Women (> 65 years-old)**

	No major complication (n=628, 83.6%)	Major complication (n=123, 16.4%)	p value
Age (years)			0.58
>65 – 70	244 (38.9)	48 (39.0)	
71 – 80	298 (47.5)	54 (43.9)	
81 – 90	86 (13.7)	21 (17.1)	
BMI (kg/m <sup>2</sup> )			0.63
< 18.5	14 (2.2)	3 (2.5)	
18.5 – 24.9	224 (35.9)	38 (31.4)	
25 – 29.9	206 (33.0)	36 (29.8)	
30 – 34.9	109 (17.5)	24 (19.8)	
35 – 39.9	43 (6.9)	12 (9.9)	
40	28 (4.5)	8 (6.6)	
Race			0.25
White	489 (77.9)	101 (82.1)	
Black	41 (6.5)	11 (8.9)	
Asian	24 (3.8)	1 (0.8)	
Unknown	74 (11.7)	10 (8.1)	
Hypertension requiring medication			0.78
Yes	381 (60.7)	73 (59.3)	
No	247 (39.3)	50 (40.7)	
Smoker			0.28
Yes	48 (7.6)	13 (10.6)	
No	580 (92.4)	110 (89.4)	
Insulin-Dependent Diabetes			0.60
Yes	81 (12.9)	18 (14.6)	
No	547 (87.1)	105 (85.4)	
History of severe COPD			0.64
Yes	29 (4.6)	7 (5.7)	
No	599 (95.4)	116 (94.3)	
History of CVA			1.0
Yes	3 (0.5)	0 (0.0)	
No	625 (99.5)	123 (100.0)	
MI within 6 months			1.0
Yes	1 (0.2)	0 (0.0)	
No	627 (99.8)	123 (100.0)	

	No major complication (n=628, 83.6%)	Major complication (n=123, 16.4%)	p value
History of TIA			0.70
Yes	9 (1.4)	2 (1.6)	
No	619 (98.6)	121 (98.4)	
Preoperative creatinine (mg/dL)			<b>0.003</b>
< 1.5	574 (96.3)	107 (89.9)	
1.5	22 (3.7)	12 (10.1)	
Preoperative hematocrit (%)			0.098
< 30	51 (8.4)	16 (13.1)	
30	558 (91.6)	106 (86.9)	
Preoperative platelet count (10 <sup>9</sup> /L)			0.166
< 450	559 (91.9)	107 (87.7)	
450	51 (8.4)	15 (12.3)	
Preoperative white blood cell count (10 <sup>9</sup> /L)			<b>0.009</b>
< 10	516 (84.7)	90 (75.0)	
10	93 (15.3)	30 (25.0)	
Preoperative albumin (g/dL)			<b>&lt;0.0001</b>
< 3.5	101 (22.7)	52 (52.5)	
3.5	344 (77.3)	47 (47.5)	
Ascites			<b>&lt;0.0001</b>
Yes	119 (18.9)	45 (36.6)	
No	509 (81.1)	78 (63.4)	

Data is reported as n(%). BMI (body mass index), chronic obstructive pulmonary disease (COPD), myocardial infarction (MI), cerebrovascular accident (CVA), and transient ischemic attack (TIA). Bolded text indicates statistical significance with p<0.05.

**Table 3**  
**Unadjusted and Adjusted Multivariable Model for Postoperative Complication among Elderly Patients**

Predictor	Unadjusted Prevalence OR		Adjusted Prevalence OR	
	OR	(95% CI)	OR	(95% CI)
Preoperative creatinine	1.2	(1.0-1.6)	1.3	(0.8-2.2)
Preoperative platelet				
>450	1.5	(0.8-2.8)	0.8	(0.4-1.8)
450	1.0			
Preoperative hematocrit	0.9	(0.9-1.0)	1.1	(0.7-1.8) <sup>I</sup>
Preoperative white blood cell	1.1	(1.0-1.1)	1.1	(1.0-1.1)
Preoperative albumin	0.3	(0.2-0.5)	0.4	(0.2-0.6)
Ascites				
Yes	2.5	(1.7-3.8)	1.7	(1.0-2.9)
No	1.0			
Current smoker				
Yes	1.1	(0.8-1.6)	1.2	(0.5-2.8)
No	1.0			
Race				
White	1.3	(0.8-2.2)	1.2	(0.6-2.2)
Non-white	1.0			

<sup>I</sup> For a 10-unit change in Hct